Amendments to the Claims

Please amend Claims 1-7, 15 and 18-19.

Please add new Claims 20-33.

Please cancel Claims 8-14 and 17.

The claim listing will replace all prior versions of the claims in the application.

Claim Listing

1.   (Currently Amended) A method of ~~treating~~ inhibiting TNFα in a human patient having a neurodegenerative ~~inflammation in a human in need thereof~~ disease, comprising administering to ~~the cerebrospinal fluid (CSF) of~~ said human patient an effective ~~TNF-inhibiting~~ TNFα-inhibiting amount of an ~~anti-TNF~~ anti-TNFα antibody or ~~TNF-binding~~ antigen-binding fragment thereof ~~sufficient to treat the neurodegenerative inflammation,~~ said anti-TNFα antibody comprising a human constant region, wherein said anti-TNFα antibody or antigen-binding fragment thereof (i) competitively inhibits binding of A2 (ATCC Accession No. PTA-7045) to human TNFα and (ii) binds to a neutralizing epitope of human TNFα with an affinity of at least 1×10^8 liter/mole, measured as an association constant (Ka), as determined by Scatchard analysis.

2.   (Currently Amended) A method of ~~treating~~ inhibiting TNFα in a human patient having a neurodegenerative ~~inflammation in a human in need thereof~~ disease, comprising administering to ~~the cerebrospinal fluid (CSF) of~~ said human patient an effective ~~TNF-inhibiting~~ TNFα-inhibiting amount of an ~~anti-TNF~~ anti-TNFα monoclonal antibody or ~~TNF-binding~~ antigen-binding fragment thereof ~~sufficient to treat the neurodegenerative inflammation, wherein said anti-TNF antibody or fragment is a chimeric TNF antibody,~~ said anti-TNFα antibody comprising a human constant region, wherein said anti-TNFα chimeric antibody or antigen-binding fragment thereof (i) comprises the antigen-binding regions of A2 (ATCC Accession No. PTA-7045) and (ii) binds to a neutralizing epitope of human TNFα with an affinity of at least 1×10^8 liter/mole, measured as an association constant (Ka), as determined by Scatchard analysis.

3.   (Currently Amended) A method of ~~treating~~ inhibiting TNFα in a human patient having a neurodegenerative ~~inflammation in a human in need thereof~~ disease, comprising administering to ~~the cerebrospinal fluid (CSF) of~~ said human patient an effective ~~TNF-inhibiting~~ TNFα-inhibiting amount of an ~~anti-TNF~~ anti-TNFα antibody or ~~TNF-binding~~ antigen-binding fragment thereof ~~sufficient to treat the neurodegenerative inflammation~~, said anti-TNFα antibody comprising a human IgG1 constant region, wherein said ~~anti-TNF~~ anti-TNFα antibody or antigen-binding fragment thereof (i) competitively inhibits the binding of ~~TNF to the TNF antibody cA2~~ A2 (ATCC Accession No. PTA-7045) to human TNFα and (ii) binds to a neutralizing epitope of human TNFα ~~in vivo~~ with an affinity of at least 1×10^8 liter/mole, measured as an association constant (Ka), as determined by Scatchard analysis.

4.   (Currently Amended) The method of Claim 3, wherein the ~~chimeric TNF~~ anti-TNFα antibody comprises a non-human variable region.

5.   (Currently Amended) The method of Claim 1, wherein said administration comprises a single or divided ~~0.1 - 100 mg/kg~~ 0.1 - 50 mg/kg dose of said ~~anti-TNF~~ anti-TNFα antibody or fragment thereof.

6.   (Currently Amended) The method of Claim 2, wherein said administration comprises a single or divided ~~0.1 - 100 mg/kg~~ 0.1 - 50 mg/kg dose of said ~~anti-TNF~~ anti-TNFα antibody or fragment thereof.

7.   (Currently Amended) The method of Claim 3, wherein said administration comprises a single or divided ~~0.1 - 100 mg/kg~~ 0.1 - 50 mg/kg dose of said ~~anti-TNF~~ anti-TNFα antibody or fragment thereof.

Claims 8.-14. (Canceled).

15. (Currently Amended) The method of ~~Claim 8, wherein the therapeutic agent is~~ Claim 1 further comprising administering to the human an effective amount of a pain control agent.

16. (Original) The method of Claim 15, wherein the pain control agent is selected from the group consisting of: paracetamol and dextropropoxyphene.

Claim 17. (Canceled).

18. (Currently Amended) The method of Claim 1, wherein the ~~anti-TNF chimeric~~ anti-TNFα antibody is of immunoglobulin class IgG1, IgG2, IgG3, IgG4 or IgM.

19. (Currently Amended) The method of Claim 1, wherein the ~~anti-TNF chimeric~~ anti-TNFα antibody is a fragment selected from the group consisting of Fab, Fab', F(ab')$_2$ and Fv.

20. (New) The method of Claim 5 wherein said single or divided dose is one selected from 0.5, 0.9, 1, 1.1, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 or 15 mg/kg per day on at least one of day 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 or at least one of week 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20.

21. (New) The method of Claim 1, wherein said Scatchard analysis comprises labeling the anti-TNFα antibody or antigen-binding fragment thereof and measuring direct binding of ^{125}I labeled anti-TNFα antibody or antigen-binding fragment thereof to immobilized rhTNFα, and wherein said antibodies are labelled to a specific activity of about 9.7 μCi/μg by the iodogen method.

22. (New) The method of Claim 1, wherein the anti-TNFα antibody or antigen-binding fragment comprises a human constant region and a human variable region.

23. (New) The method of Claim 1 wherein said anti-TNFα antibody or antigen-binding fragment comprises at least one human light chain and at least one human heavy chain.

24. (New) The method of Claim 1, wherein said anti-TNFα antibody or antigen-binding fragment is administered to the human by means of parenteral administration.

25. (New) The method of Claim 1, wherein said anti-TNFα antibody or antigen-binding fragment is administered to the human by means of intravenous administration, subcutaneous administration or intramuscular administration.

26. (New) The method of Claim 23, wherein the light chain comprises all antigen-binding regions of the light chain of A2 (ATCC Accession No. PTA-7045).

27. (New) The method of Claim 23, wherein the heavy chain comprises all antigen-binding regions of the heavy chain of A2 (ATCC Accession No. PTA-7045).

28. (New) The method of Claim 23, wherein the light chain comprises all antigen-binding regions of the light chain of A2 (ATCC Accession No. PTA-7045) and the heavy chain comprises all antigen-binding regions of the heavy chain of A2 (ATCC Accession No. PTA-7045).

29. (New) The method of Claim 1, further comprising administering a composition comprising the anti-TNFα antibody or antigen-binding fragment of Claim 1 and a pharmaceutically acceptable carrier.

30. (New) The method of Claim 1, wherein said anti-TNFα antibody or antigen-binding fragment has specificity for a neutralizing epitope of human TNFα.

31. (New) The method of Claim 1, wherein said anti-TNFα antibody comprises a non-human variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NO:3 and SEQ ID NO:5.

32. (New) The method of Claim 31, wherein the non-human variable region is murine.

33. (New) The method of Claim 32, wherein the non-human variable region comprises a polypeptide encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:4.